IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: CULLEN, Breda

Serial No.: 09/601,806 **Group Art Unit:** 1653

Filed: November 30, 2000 **Examiner:** C. Lyon

Title: Sterile Complex Therapeutic Peptide Bond to a Polysaccharide

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

PRELIMINARY AMENDMENT

In response to the Office Action of March 26, 2003 (copy enclosed), please be informed that this is a request for regular continued prosecution.

We require additional time to review the office action with the inventor.

IN THE SPECIFICATION:

Specification remains the same as the original filed application filed under 35 U.S.C371 on 30.11.00 having a filing date of 12/6/1999 of PCT/GB99/04094

Respectfully submitted,

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UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/601,806	11/30/2000	Breda Cullen	JIM-454	3588

7590 03/26/2003

Audley A Ciamporcero Jr
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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 03/26/2003

8

Sep 26, 2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Copy sent to Jamie Harrington on 4.11.03 Signed D. Velasquez

Response Due @ 6.26.03

9.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/601,806	CULLEN ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

CPA STATUS ACCEPTABLE

1. The request filed on 1/16/03 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/601,806 is acceptable and a CPA has been established. An action on the CPA follows.

ACKNOWLEDGMENT FOR PRIORITY, IDS, STATUS OF THE APPLICATION AND CLAIMS

2. This application is filed under 35 U.S.C. 371 on 11/30/00 having a filing date of 12/6/1999 of PCT/GB99/04094. Acknowledgment is made of Applicant's claim for priority based on United Kingdom Application Number GB 9826897.2 having a filing date 12/7/1998. Receipt is acknowledged of Certified Copy of United Kingdom Application Number GB 9826897.2 and papers submitted under U.S.C. § 119, which papers have been placed of record in the file. Also, the Information Disclosure Statement (IDS) and Form PTO-1449 filed 8/3/00 are acknowledged, entered and considered. Claims 1-33 are present for examination.

ABSTRACT MISSING

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

OBJECTIONS TO TRADEMARKS AND THEIR USE

4. The use of the trademarks "INTERCEED®", "SURGICEL®", "STERAD®", "FORMOL®", "BIOLINX®" and "TRITON®" have been noted in this application. Although, the use of trademarks are permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in a manner which might adversely affect its validity as trademarks.

Further, the specification which specifies the generic terminology should include published product information sufficient to show that the generic terminology or the generic description are inherent in the article referred by the trademarks. These description requirement are made because the nature and composition of articles denoted by trademarks can change and affect the adequacy of the disclosure.

OBJECTION TO IMPROPER MULTIPLE DEPENDENT CLAIMS

5. Claims 7-22 and 27-31 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and/or cannot depend from any other dependent claims. See MPEP § 608.01(n). However, the claims been treated on the merits and interpreted as dependent solely from the first recited claim from which the claims depend.

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "mixtures thereof" after Markush format as recited in claims 1, 4, 23 and 32 makes the claims indefinite because in regard to claims 1, 23 and 32, the polysaccharides selected have 4 components, namely, cellulose derivatives, chitin, chitosans and galactomannans, and it is not clear how these 4 components are mixed with each other. The specification or the claims fail to provide guidance as how and/or which components are mixed with the amounts necessary to mix them against each other in the manner claimed.

With respect to claim 4, eight growth factors are recited in the claim and it is not understood how these 8 components would result in a sterile composition having mixtures thereof for the reasons discussed above. Thus, since the metes and bounds of "mixtures thereof" are not set forth in the disclosure nor in the claims, deletion of the term "mixtures thereof" would obviate this rejection.

Further, in claim 4, there is inconsistency in the recitation "mixtures thereof" and "growth factor" because "mixtures" is plural and "growth factor" is singular.

Claims 7-22 and 27-31 are indefinite for being improper multiple dependent claims because a multiple dependent claim is supposed to depend in the alternative only. Also, a multiple dependent claim shall not serve as a basis for any other multiple dependent claim, either directly or indirectly. These limitations help to avoid undue confusion in determining how many prior claims are actually referred to a multiple dependent claim. Thus, claims 7-22 and 27-31 are improper multiple dependent claims for the above reasons.

Claims 9, 10 and 21 recite the acronym "ORC" and "nORC" (claim 9). Use of the full terminology at least in the first occurrence would obviate this rejection.

CLAIMS REJECTION-35 U.S.C. § 103(a)

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watt et al. (GB Patent No. 2,314,842) taken with Orsolini et al. (GB Patent No. 2,257,909) or Cini et al. (U.S. Patent No. 5,705,485) or Finkenaur (U.S. Patent no. 4,717,717).

The reference of Watt et al. (GB Patent No. 2,314,842) discloses like the instantly claimed invention a sterile composition comprising a complex of a therapeutic peptide and polysaccharide and to a method of preparation the sterile composition thereof (See e.g., abstract). The reference clearly discloses the preparation and uses of complexes of structural proteins such as collagen, fibronectin, fibrin, laminin, elastin, growth factors with polysaccharides such as oxidized regenerated cellulose (ORC), cellulose derivatives, chitin, chitosans, etc. at the weight ratio of protein to ORC from 1:99.99 to 99.99:1 (See e.g., page 3, lines 12-29), wherein the complexes are useful for wound dressing and the like, and exhibit useful binding to growth factor particularly to platelet derived growth factor (PDGF) (See e.g., page 5, lines 7-22). The reference also teaches a process for the preparation of the complex by providing an aqueous dispersion of a protein; and/immersing or dispersing OCR in the aqueous dispersion; following by removing water from the aqueous dispersion to leave a material comprising protein complexed with oxidized regenerated cellulose (ORC) (See e.g., page 6, lines 6-21). The water can be removed from the aqueous dispersion by filtration, evaporation, or freeze-drying (lyophilization) or solvent-drying to produce the material in the from of a sponge (See e.g., abstract; page 1, lines 3-6; page 2, lines 25 to page 5, lines 22; page 6, lines 6-29; Figures 2-3; Example 4, claims 14, 23 and 26). Thus, the reference clearly teaches the preparation that may be used for topically

administration wherein the composition is sterilized prior to administration as the therapeutic peptide are stabilized against decomposition during sterilization by being formulated with biopolymer such as structural protein or polyanionic polysaccharide.

The reference differs from claims 1-33 in not teaching a) sterilization with ionizing radiation, b) wherein the peptide comprises a growth factor having human mitogenic or angiogenic activity, c) the complex further comprises a free radical scavenger, and d) wherein the complex is administered intravenously. Although, the primary reference of Watt et al. clearly teaches the use of complexes for wound dressing and the like which is applied topically in animals including humans, the complexes are sterilized since they are applied *in vivo*, however, Orsolini et al. (GB Patent No. 2,257,909) clearly disclose the sterilization of complexes comprising a therapeutic peptide and a polysaccharide by gamma ray sterilization and the suspension of the complexes in an appropriate sterile vehicle (See e.g., page 8, last paragraph to page 9, first paragraph; and Example 7). Further, the reference of Cini et al.(U.S. Patent No. 5,705,485) on col. 1, lines 63-66 discloses an aqueous gel formulations for topical or incisional wound healing comprises an effective wound healing amount of a polypeptide growth factor having human mitogenic or angiogenic activity. Furthermore, the reference of Finkenaur (U.S. Patent No. 4,717,717) teaches the use of a stabilized medicinal complex comprising a therapeutic peptide and a polysaccharide and wherein the complex further comprises as an additional agent anti-oxidants (i.e., free radical scavenger) and useful for in eye drop formulation, salves for wound healing, gel formulations, foams, and the like (See e.g., col. 3, lines 18-32).

Thus, in view of the above, given the teachings of the primary reference, one of ordinary skill in the art would have been motivated at the time the invention was made to adapt the above scheme of sterilizing with ionizing radiation, or use of a peptide which comprises a growth factor having human mitogenic or angiogenic activity and sterile composition further comprising a free radical in a sterile formulation comprising a complex of therapeutic peptide and a polysaccharide as taught by the secondary references. Further, such features are known or suggested in the art (particularly, the sterilization by gamma rays, use of a growth factor having human mitogenic or angiogenic activity and use of a radical scavenger) as seen in the secondary references, and including such features into the method and/or composition/product of primary reference would have been obvious to one having ordinary skill in the art to obtain the known and recognized functions and advantages thereof.

With respect to claim 17, the claim is directed to intravenous administration, however, each of the prior art teaches the topical administration of the same complex for the same purpose of treating animals including humans; thus, in view of this, it is the Examiner's position that the selection of suitable route of administration is deemed to be within the scope of those skilled in the art to which this invention pertains, and as such, one of ordinary skill in the art would easily adjust the route of administration depending on the specific agent in question (i.e. if the formulation is liquid or solid or semi-solid or powder, etc.), conditions to be treated (i.e. skin versus internal, etc.) and the amount of the agent to administered.

With respect to claim 22, the claim is in product-by-process format and as such, it is the novelty and patentability of the instantly claimed product that need be established and not the recited process steps, In re Brown, 173 USPQ 685 (CCPA 1972); In re Wertheim, 191 USPQ (CCPA 1976). Further, the prior art described the product as old, In re Best, 195 USPQ 430, 433 (CCPA 1977); (See MPEP 706.03 [e]). Hence, the burden of proving that the process limitation makes a different product is shifted to the Applicants, In re Fitzgerald, 205 USPQ 594.

Therefore, in view of the above and in view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated to employ a sterile composition sterilized with ionizing radiation comprising a complex of a therapeutic peptide and polysaccharide and a method of preparation the sterile composition thereof in the manner claimed in claims 1-33, absent of providing sufficient objective factual evidence or unexpected results to the contrary.

CONCLUSION AND FUTURE CORRESPONDENCE

8. No clam is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Mohamed/AAM

March 21, 2003

Revised Notice*
AMENDMENTS MAY NOW BE SUBMITTED IN REVISED FORMAT

The United States Patent and Trademark Office (USPTO) is permitting applicants to submit amendments in a revised format as set forth below. Further details of this practice are described in *AMENDMENTS IN A REVISED FORMAT NOW PERMITTED*, signed January 31, 2003, expected to be published in *Official Gazette* on February 25, 2003 (Notice posted on the Office's web site at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). The revised amendment format is essentially the same as the amendment format that the Office is considering adopting via a revision to 37 CFR 1.121 (Manner of Making Amendments). The revision to 37 CFR 1.121 (if adopted) will simplify amendment submission and improve file management. The Office plans to adopt such a revision to 37 CFR 1.121 by July of 2003, at which point compliance with revised 37 CFR 1.121 will be mandatory.

Effective immediately, **all** applicants may submit amendments in reply to Office actions using the following format. Participants in the Office's electronic file wrapper prototype[1] receiving earlier notices of the revised practice may also employ the procedures set out below.

REVISED FORMAT OF AMENDMENTS

Begin on separate sheets:
Each section of an Amendment (e.g., Claim Amendments, Specification Amendments, Drawing Amendments, and Remarks) should begin on a separate sheet. *For example*, in an amendment containing a.) introductory comments, b.) amendments to the claims, c.) amendments to the specification, and d.) remarks, each of these sections must begin on a separate sheet. This will facilitate the process of separately indexing and scanning of each part of an amendment document for placement in an electronic file wrapper.

Two versions of amended part(s) no longer required:
The current requirement in 37 CFR 1.121(b) and (c) to provide two versions (a clean version and a marked up version) of each replacement paragraph, section or claim will be waived where an amendment is submitted in revised format below. The requirements for substitute specifications under 37 CFR 1.125 will be retained.

A) Amendments to the claims:
Each amendment document that includes a change to an existing claim, or submission of a new claim, **must include a complete listing** of all claims in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.

(1) The current status of all of the claims in the application, including any previously canceled or withdrawn claims, must be given. Status is indicated in a parenthetical expression following the claim number by one of the following: (original), (currently amended), (previously amended), (canceled), (withdrawn), (new), (previously added), (reinstated – formerly claim #_), (previously reinstated), (re-presented – formerly dependent claim #_), or (previously re-presented). The text of all pending claims under examination must be submitted each time any claim is amended. Canceled and withdrawn claims should be indicated by only the claim number and status.

(2) All claims being currently amended must be presented with markings to indicate the changes that have been made relative to the immediate prior version. The changes in any amended claim should be shown by strikethrough (for deleted matter) or underlining (for added matter). An accompanying clean version is not required and should not be presented. Only claims of the status "currently amended" will include markings.

(3) The text of pending claims not being amended must be presented in clean version, i.e., without any markings. Any claim text presented in clean version will constitute an assertion that it has not been changed relative to the immediate prior version.

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[1] The Office's Electronic File Wrapper prototype program is described in *USPTO ANNOUNCES PROTOTYPE OF IMAGE PROCESSING*, 1265 *Off. Gaz. Pat. Office* 87 (Dec. 17, 2002) ("Prototype Announcement"), and applies only to Art Units 1634, 2827 and 2834.